

Figure 1A

ACC OTC GCT GGG GGG CGC TTC ACA GAG GAG TGG TAC GCG GGG CAC TGG GCC ACA GGA ACA GGA ACT GGG GGC GAC TGG GGC GAC TGG GGC GGT TGT CCTT TCA CCC T $^{\circ}$ $^{\circ}$:100 AAA GGA GGC TGT CCT: GCT GTG GTG GTG AAG GCC GGT TAC CAG ACA ATG AGT ATC CTG GCC ATG $^{\prime\prime\prime}$ TT CCT GCG ACA CAA GCA CAC GCC GAC $^{\prime\prime\prime}$ TT CCT GCG ACA ATG GTC TGT TAC TCA TAG GAC GGG TAG $^{\prime\prime}$ K G C C P A V P $^{\prime\prime}$ K A R Y Q T M S I L P MS :300 GAG CTN TAT AAG GAG TIT GCA GAA TAT GTA ACC AAC CAC WAG GGC ATG CTO TGT GCC GTC CTC
GTG GAT ATA TTC CTC AAA CGT CTC ATA CAC TGG TTC GTG ATG GGC TAC GAC ACA CGG CAC GAC
E L Y K E F A E Y V T N H Y R M L C A V L GAG CGG GAA GAC CTC AVA TTC CGC GAG AAC ACG CTC GCC ACT AAA CCC AVA GAA GAC TAU ATG CTC GCC CGC CTC GTC GAG TAT CAAG GAC CGC GTC TTC GCC GAG CGG TGA TTT CGG WAT CTT CTC ATA TAAC E R Ξ H L I Ξ R Ξ N T L A T R A I E E Y BAGA CTC ATT GGC CAG AAA TAC CTC AAG GAT GCC ATT GGG CAG TTC ATC CGG GCT CTC TAT GAA TCT GAC TAA CCG GYC TTT ATG GAG TTC CTA CGG TAA CCC CTC AAG TAG CCC CGA CAC ATA CTT R L I G Q K Y L K D A I G Y F I H A L Y E GCC AAC CTG CGG ALTG TGC TGT GAG TTG GCC CHG TGC AAC GTG GTC AAC TCG GAT TGC GTG TTC CGG TTG GAC GCC TAC ACG ALA CTC AAC GAC GAC ACG TTC CAC CAC TTG AGG GTA ACG CAA AAG A N L R M C C Z L A L C K V V N 5 H C V F> CCG AGG GAG CTG AAC GAG GTG TTT GDA TOA TOC CGG CTG GCC TGT GCA GAG GGG GGC CGG GAG GGG TCC CTT CAC AAA CCT ACT ACC GCC GAC GCG ACA CGT CTC GCC GCC GCC CTT P R B L X B V P A S W R L R C A R R G R B GAC ANT GOT GAC AGG OTG ACC AGG GCC TCG CTC THE CTC CGC THE CTC TCC CCG GCC ATC ATG
CTG TAA CGA CTG TCC GAC TAG TCG GCC AGC GAG AAG GAC GCG AAG GAC ACG GGC CCC TAG TAC
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Figure 1B

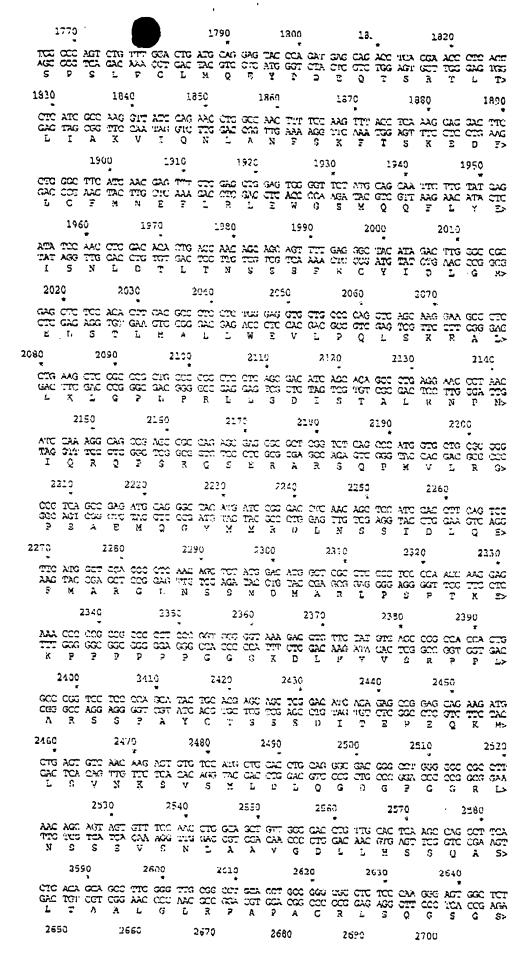


Figure 1C

ATE COC CITE ACC CAS ATE COT CITE ACT AL COMMENT OF THE COMMENT OF TOO ATC ACA COA אכם שבה תפוד כבון AAGH 27/20 274C O O D R I R D S F O N R D I R R N A A D D G PROCESS CONTRACTOR CON 290C -294C THE AGO AND ACC GAG GAC CTC TOT: ACA COO GTC OUT AND WES COS SEC THE ATT CAC ATA TOO TO TOO TOO GAG AGA TOT CAC CAG CGA THE GGG GGA CGC CGG AGA TAAG GAA GTC Y S X 3 E D L S T Q V P X P P A A S I L E> 293C AGO CHO AGO TAC HOT GAT GAG TIT GOA CHO THIT GOT ACT GAT THIT ACC CGT CGG CHO CTC TOX TOG GIG TOG ATG TOA CITA CITO AAA COT GGG AGA COA TOA CITA AAA TOG GCA GCT GITO GAG AGT B B S Y S D E F G P S G I D F II A R R Q L S> 336C GRU TOG GAG CTG ACT GTA GGC TGG GTR TRI AAT AAG CCT GAC CUG TGT GOT GAC ATC GAG AGT CAC AGG TTA TAC GGA GTG GAC AGG CGA CTG TAC CTC ACA A S 3 3 T V X W V S N W 2 3 R 2 R 2 A D I 3 S 348ú

Figure 1D

CTG GAC AGG GTG AAG GAG TAC GAG GAG GAG GAC CAC AFC CAC TCA CTG AAG GAA AGG GTA CAC ATG GCG GAC CTG TCC CAC CTC CTC CTC CTC GAG GAT AGT GAC TTC CHH WCC GAT GTG TAC AGG TC CTC TAC AGG AND COS ANG CTG GAA GAG TRIC GAG COG AGG ATT GTG TCC CAG GAA GAG CAG AGG AGG AAG ATT TTG GCC TTG GAG GTT CTC ATG CTG CCC TCC GAG GAG AGG GTG GTT GTG GTG TCG TCG TCG TCG TCG N R R T T T T T R R R R L L S Q E E Q T S X L 369C # 409C ACT GGA COT GAC CAA GGG ACA GGG GGA TTG TOT COO TEA ACG COF COT TGG GGA ACC CAT CTG
TGA CCT GGA GTG GTT GCG TGT GGG GCT AAC AGA GGG AACT TGG GGA ACC CCT TGG GTA GAC
TG G R H O G T A G L S P L T P P W G T H L>

Figure 1E

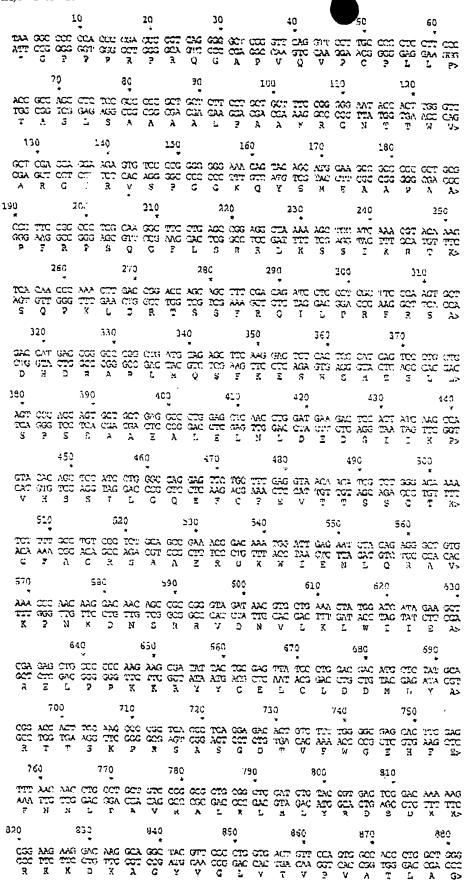


Figure 2A

COC CAC THE ACA GAG CAC TAKE TAKE CHE GIFF ACT CHE CAL ACA COA ACT CHE GOE GIFF GOE GIFF GOE GIFF GOE GIFF ACT CHE ACA COC CHE ACA COC CHA ACA COC CHE ACA COC CHA ACA COC CHE ACA COC CHA CTC ATA TTC CGC GAG AAC ACG CTM GGC ACT AAA GCC AFA GAA GAG TAN ATG AGA CTG ACT GGC GAG TAN AAG GCG GTG TAT GGC GAG TAN TTT GGG TAN CTT CTC AMA TAC TCT GAC MAA CCC MAA CCC L L M A C L L GA CCC L A C L M A C L L GA TOT GAA GTA GAC 000 $\lambda 10^{\circ}$ $\lambda 60$ 000 $\lambda 10^{\circ}$ $\lambda 60$ 000 $\lambda 60$ 000 $\lambda 60$ 000 $\lambda 60$ 000 $\lambda 60$ 000 000 $\lambda 60$ 000 0AGG CTG ATC AGC GCC TCG CTC TTC CTC CTC CTC TCC CCC GCC ATC ATC ACG CCC AGT CTC
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K 7, I 8 A 8 L F L R F L C P A I M S P S L WIT ATC CAG AAC CTG CCC AAC TIT ICC AAG TIT ACC TU AAG GAG GAG TIC CTG GGC TIC ATC CAA TAG GAC GTC TTG GAC CGG TAG AAA AGG TTC AAA TGG AGT TTC CHI GTG AAG GAC CCG AAG TAC V I Q N L A N F S K F T S K 2 D F L 4 A M 4

Figure 2B

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Figure 2C

SEC CHI SEL CIN CIT. LEE LEE CHE CHE C are are ary the 274C GAG GAG CITC TOT ACA GGG GTC COT AAG CTC CCT GGG GGC TOC ATC CITT CAC AGC CAC AGC TAC CTC CTC GAG AGA HGT CCC CTC GGA GGA GGG GGA GGC CGC AGG TAG GAA GTC TCG GTC TCG ATC Z D L S T G V P K P P A A S I L I S H S V> 302C CITA TITY CAN THE COE GAA COA AGE THE OUT COT GOO COE COA CAG AGE CITE AGE AAA CAG AGE CITE AGE AAA CAG AGE CITE AGE AGA CAG AGE COE GITE GAG SCC NGT ATT GOG COD ACC CGG SCC NGT ATT GTG GGA GGG GTT GGG GGG STC AAG CCC TCC CCC TCC CCC TCC TCC CCC TCC T ATC ACC AAG CAG CAG TOU CRG ACT COA TOO ACG CTG AAG CCC ACG ACG CCG TOO GAG CCG
TAG TGG TTC GTC GTA AGG GTC TGA GGT AGG "GC GAC TTC GAG TTC GAG TAG GCC CTG AGG
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Figure 2D

36BC ACT AGC CCA CCC AGG AVG ACA GAG GVC CTT CCC TGT GCA CCC TAC CCC GGC CCA CCC AGG GVC TGA TCC TCC GGC CCA CCC AGG GVC CAG TCC TCC GAG GCC GCC GCC GCC GCC CCA CCC AGG GVC CAG TCAA GOG ACA GOG GOA THG TOT COC TTA ACU COT COT TOD GOD ACT CAT CTG TOA ACC COA GTG
GTT COC TOT CGC CCT AAC ACA GOG AAC TGC GGA GGA ACT CGG TGG GNA GAC AGT TGG GGT GAC
G G T A G Z S Z L T Z Z W G T H L S T Z Z L CAC ACA CAC CCC TTC ACT CIV GGG TGC TAT UCT CAT CCT CTC TCT CTC CCG AAG TCA CAC CCC ACG ACA CGG GTA GGA H T C C Y F H F

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Figure 3D

Figure 3E

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121	ttskprsasgdtvfwgehpefnnlpavralrlhlyrdsdkxxxxdkagvvglvtvfvatl	180
181	AGRHFTEQWYFVTLFTGSGGSGGSGGGGGGGGGGGGGGGAGACGCFAVRLKARYQTMSILF	240
241	melykefaeyvtnhyrmlcavlefalnvkgkeevasalvrilgstgaakdflsdmamsev	300
301	DRFMEREHLIFRENTLATXAISEYMRLIGQKYLKDAIGES IRALYESEENCEVDPIXCTA	360
361	SSLAPHOANLRMCCHLALCRYVNSHCVFPRELXEVFASWRLRCAERGREDIADRLISASL	420
421	FLRFLCPAIMSPSLFGLMQEYPDEQTSRTLTLIAKVIQNLANESKFTSKEDFLGPMNEFL	480
481	elengsmooplyeisnidtlinsssfegyidlg <u>rels</u> tlenllwevlpolskenllkig?	540
541	LPRILEDISTALRNPNIOROPSRQSERARSQPMVLRGPSAEMCGYMMPDLNSSIDLQSFM	600
601	Arglnssm <u>omarləs</u> ptx=x?ppppgggrdlfyvsrpplarss?ayctsssdite?eqk	660
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721	GSGSSITAAGMRLSQMGVTTDGV?AQQLRI?LSFQNPLFHMAADG?G?9AGHGGSSGHG?	780
781	PSSHHHHHHHHHHRGGE?PGDTFAPFHGYSKSEDLSTGVPKPPAASILHSHSYSDEFG?S	840
841	GTDFTRROLSLQDNLQHMLSPPQITIGPQRPAPSGPGGGGGGGGGGGGGGPPPLQRGKS	900
901	QQLTVSAAQK? <u>RPSS</u> GNLLQS?E?SYG?AR? <u>BCOS</u> LSKEGSIGGSGGGGGGGGCK?SI	960
961	tkoksotpstlnptmpasertvawvsnmphlsadiesahier <u>efy</u> kl <u>kev</u> sksndesrld	1020
1021	RV <u>KEYEEEIHSLKERLHMSNRKLEEYERRILLSO</u> EEQTSKILMQYQARLEQSEKRLRQQQV	1080
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Figure 4A

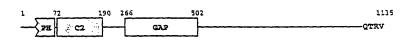


Figure 4B

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Gapsyn	286	GKAKDFLSDMAMSEVDRFMERE-HLIFRENTLATKAIEEYMRLIGQKYLKDAIGEFIRALYE	347
rn GAP	755	KLESLLLCTLNDREISMEDEATTLFRATTLASTLMEQYMKATATQFVHALKDSILKIME	815
hs NF1	1251	HLLYQLLWNMFSKEVELADSMQTLFRGNSLASKIMTFCFKVYGATYLQKLL-DPLLRIVI	1311
Gapsyn	348	SEENCEVDPIKCTAS-SLAEHQANLRMCCELALCKVVNSHCVFPRELKEVFASWRLR	403
rn GAP	816	SKOSCELSPSKLEKNEDVNTNLAHLLSILSELVEKIFMASEILPPTLRYIYGCLQKS	872
hs NF1			1372
		++ +	
GAPSYN	404	CAERGREDIADRLISASLFLRFLCPAIMSPSLFGLMQEYPDEQTSRTLTLIAKVIQNLAM	463
rn GAP			934
hs NF1		vsqrfqqnsigAvgsamplrfinpaivspyeagildkxppprierglklmskilqsian	1430
		++	
GAPSYN	464	FSKFTSKEDFLGFYNEFLELE-WGSMQQFLYEISNLDTLT	502
rn GAP	935	LVEPGAREPYMEGVNPFIKSN-KERMIMFLDELGNVPELP	973
hs NF1			1469
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Figure 4C

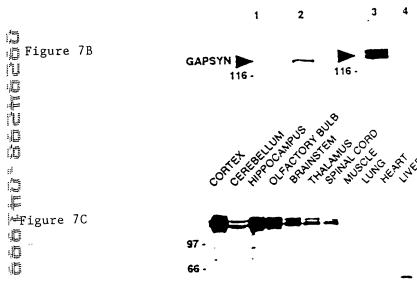
Pleckstrin Homology(PH) Domain Alignment

Hs pl20 Dm GAP1	471 759	FKESHSHESL FYKNIVKKGY PVLLKEGEGL MEPKRIREGY	LLKKGKG MTKYPTSRKR	KRWKNLYF FGRQFKQRHF	ILEGSDAQLI RLTTHSLS	YFESEKRATK YAKSKGKQ	5 1 80
Hs p120 Dm GAP1	516 805	P PKGLIDLSVC PICDIPLQEI PKGMIPLKGS	SVYVVIIDSLF ASVEQLKDKS	GR.PNCFQIV FKMQNCFKIV	VQHFSEEHYI HNDRS	FYFAGETPEQ LIVQTTNCVE	56 84
Hs p120 Dm GAP1	565 850	RDKWIENLQR AEDWMKGLQA EREWFDLLHK RDAWVRDINK	FCNLRKSSPG ICLMNSIRMQ	584 869			

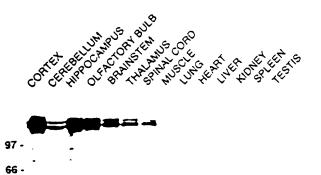
C2 Domain Alignment

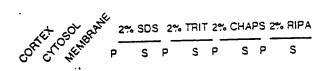
	Hs p120 Rn Syt II	592 151	QVSSLVLH DYDFQANQLT	IEEAHKLP VGVLQAAELP	VKHFTNP ALDMGGTS D P	YCELCL YCNIYL YVKVFLLPD. YVKLHLLPGA	NSVQVAKTH. .KXXKYETKV	629 198
			•					
Ę	SynGAP-a	282	KPRSASGDTV	fwgehfefnn	LP.AVRALEL	HLYRD.SDKK TLSNKT TLVMAIYDFD	RKKDKAGYV G	329
:F	Hs >120	630	AREGQNP	VWSKEPVPDD	LPPDINRFEI	TLSNKT	.XXSKDPDIL	571
	Rr. Syt II	199	HRKTLNP	AFNETFTFK V	PYQELGGK	TLVMAIYDFD	RF.SKHDIIG	242
	Bt Rab 3A	461	LRNTRNP	IWNETLVYHG	I.TDEDMQPK	TLRISVCDED	KF.GHNEFIC	505
**************************************	SynGAP-a	330	LVTVPVAT		.LAGRHFTEO	WY.PVT.LPT	354	
: ==	Hs p120	672	FMRCOLSR		LCKGHATDE	WFLLSSHIPL	698	
	Rn Svt II	243	EVKVPMNTVD		.LGOPIEE	WRDLOGG.	266	
	Bt Rac 3A	506	ETRFSLKKLK	PNQRK.NFNI	CL. ERVIPM	WY.PVT.LPT WFLLSSHIPL WRDLQGG. KRAGTTGSAR	542	

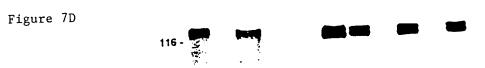




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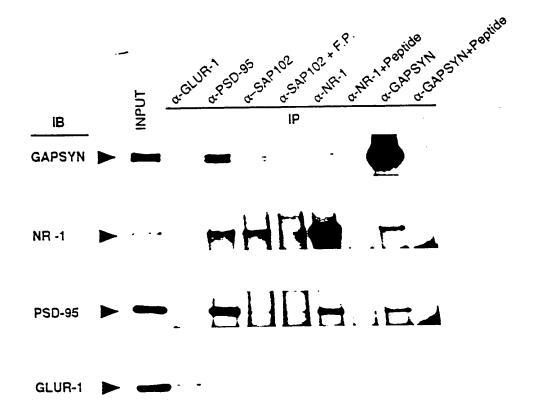


Figure 8

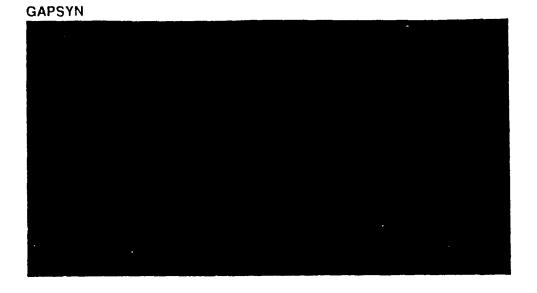
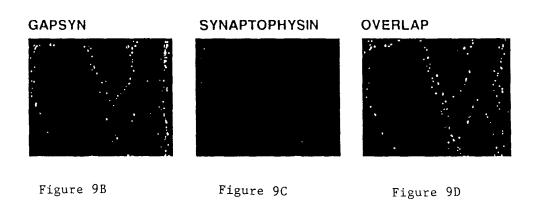


Figure 9A



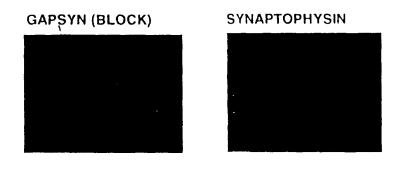
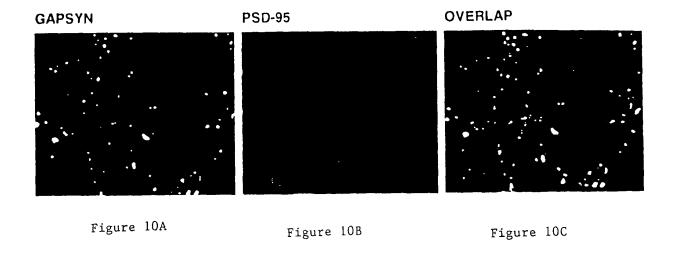
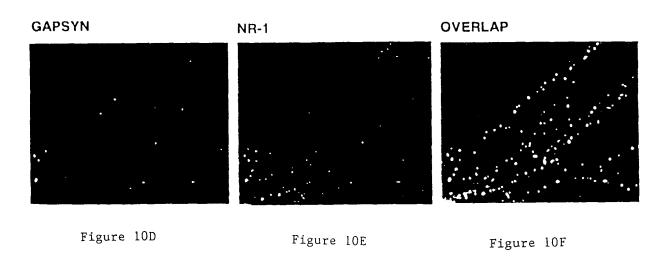


Figure 9E

Figure 9F





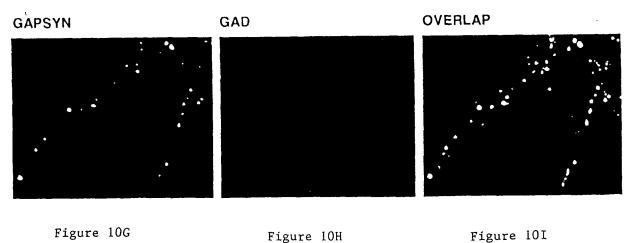


Figure 10G Figure 10H

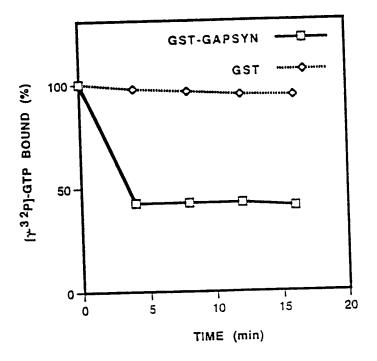


Figure 11